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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|----------------------|------------------|
| 09/824,787 | 04/04/2001 | Maurice Zauderer | 1821.0040001/EKS/TJS | 2970 |

26111 7590 09/30/2005

STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

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| EXAMINER |
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HARRIS, ALANA M

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| ART UNIT | PAPER NUMBER |
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1643

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/824,787

Applicant(s)

ZAUDERER ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☒ Claim(s) 123, 158 and 166 is/are allowed.
- 6) ☒ Claim(s) 84, 119, 121, 164, 165 and 210-215 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>04/22/05; 07/06/05</u> | 6) <input type="checkbox"/> Other: _____ |

Continuation of Disposition of Claims: Claims pending in the application are 47-51,53,56-66,68,69,74-78,80,82,84-89,91,94-104,106,107,112-116,118-121,123-128,130,133-143,145,146,151-155,157-159 and 164-215.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 47-51,53,56-66,68,69,74-78,80,82,85-89,91,94-104,106,107,112-116,118,120,121,124-128,130,133-143,145,146,151-155,157,159 and 167-209.

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DETAILED ACTION

Response to Arguments

1. Claims 47-51, 53, 56-66, 68, 69, 74-78, 80, 82, 84-89, 91, 92, 94-104, 106, 107, 112-116, 118-121, 123-128, 130, 133-143, 145, 146, 151-155, 157-159 and 164-214 are pending.

Claims 47-51, 53, 56-66, 68, 69, 74-78, 80, 82, 85-89, 91, 94-104, 106, 107, 112-116, 118, 120, 124-128, 130, 133-143, 145, 146, 151-155, 157, 159 and 167-209, drawn to non-elected inventions are withdrawn from examination.

Claims 84, 119, 121, 123, 158, 164-166 and 210-214, which read on the elected species, nn. I-105 to V-113 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained and New Grounds of Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claims 84, 119, 121, 164, 165, 210-214 and newly added claim 215 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained and made.

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Applicants aver in the Remarks submitted July 12, 2005 on page 21 the test for written description requirement and allege that their "... claims do not read on a genus more varied than that encompassed by a nucleotide sequence comprising an EST sequence", see page 29, last complete sentence. Applicants arguments include Court opinions, which they allege support their case of meeting the requirements of written description. These points of view have been carefully considered, but found unpersuasive.

Applicants' arguments are similar to those made in the Remarks filed October 15, 2004. The rejection is maintained and made because it still stands that claims 84, 119, 121, 164, 165 and 210-215 broadly claim a fusion protein comprising at least one C35 peptide epitope defined as I-105 to V-113 of SEQ ID NO: 2 and a polypeptide selected from the group consisting of a heterologous epitope, a heterologous signal sequence, a heterologous functional domain, part of the constant domain of an immunoglobulin, and a marker sequence. The written description in this instant case only sets forth polypeptide, SEQ ID NO: 2 consisting of 115 amino acid residues and including the defined epitope consisting of I-105 to V-113. The written description is not commensurate in scope with the claims drawn to a fusion protein comprising the defined sequence of I-105 to V-113 and arbitrary polypeptides. There is no size limit for the fusion protein. There is no defined structure and function established for the claimed fusion protein. These additional amino acids are not adequately described therefore one of ordinary skill in the art does not have explicit information regarding for example, the amino acid residues, the size of the polypeptides, the

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structure of the polypeptides. Consequently, the fusion protein comprising the defined C35 peptide epitope and undefined amino acid sequences is not exemplary of Applicants' possession of the claimed fusion polypeptide.

At the time the application was filed Applicants only had possession of SEQ ID NO: 2 (consisting of 115 amino acids), comprising the amino acid epitope, I-105 to V-113 and not fusion polypeptides that include undefined amino acid sequences. The fusion protein potentially contains at least 107 amino acids that have not been described. Likewise the fusion protein that comprises one C35 peptide epitope is surrounded by amino acids not described in the specification. The broad claim reads on a plethora of polypeptides of any length, hence there is no sufficient evidence presented in the Remarks or of record of Applicants' possession of such a huge group of polypeptides. And while Applicants do not have to list every species within a claimed genus, there must be a representative number of species presented. The specification does not evidence the possession of all the possible fusion proteins the claims encompass. Applicants should review the Official Gazette, January 30, 2001.

Based on the analysis set forth above and of record the full breadth of the claims do not meet the written description provision of 35 U.S.C. 112, first paragraph.

4. The rejection of claims 84, 119, 121, 164, 165, 210-214 and newly added claim 215 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed

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invention is maintained and made. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants note the test of enablement and assert "...the specification provides adequate guidance as to how C35 peptide epitopes and fusion proteins can be used.", see page 33 of Remarks. Applicants state "the claims are not overly broad in light of the extensive disclosure of the various aspects of the invention.", see page 37. Applicants also have submitted three papers, which establish epitopes within larger and unrelated proteins can be processed properly. These papers, points of view and the specification have been carefully considered but found unpersuasive.

Example 2 of paragraphs 254-256 broadly expound on the subject title, C35 specific CTL are cytolytic for C35 positive breast tumor cells. Applicants point these sections of the specification for support for enablement. It not clear from these sections which amino acid residues were considered as the C35 peptides that facilitate killing of the breast tumor cells, nor is it clearly indicative of the use of a peptide defined as I-105 to V-113 amongst undefined sequences resulting in a fusion protein would reasonably facilitate or impart the functions as dictated by the specification. And while Applicants note that the fusion protein may include a number of art known sequences, such as a heterologous functional domain there is no description of the function this domain must have and whether or not its function would be conducive to killing the said cells. Applicants submit that testing is necessitated to confirm that MHC-restricted,

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human tumor antigen-specific T cells can be induced by C35. Likewise, a consideration must be the presentation of the C35 peptide in the context of the fusion protein. Applicants' specification does not provide sufficient guidance on wherein the fusion protein the peptide should be placed which is germane to its use. Del Val's findings: "amino acid that flank an antigenic sequence in the protein can have a profound positive or negative effect on antigen processing and presentation" and "differences in presentation efficiency reflected differences in the amount of naturally processed peptide" reflect the amount of experimentation that must be applied by those skilled in the art to determine the applicability of the claimed invention, see page 1145, second column, paragraph before Results section, IDS reference AS submitted July 6, 2005. The quantity of experimentation in this area is extremely large since heterologous epitope, a heterologous signal sequence, a heterologous functional domain, part of the constant domain of an immunoglobulin and a marker sequence have not been clearly defined by the specification. Moreover, it is not clear what the limits are of a "part of a constant domain". This recitation in itself reads on a couple of amino acids or many amino acids. While it is clear Applicants desire to implement these fusion proteins in the treatment of C35-specific cancers, in diagnostic and prognostic applications it would require significant study to identify, make and use the exponential amount of fusion proteins that are applicable to treatment, diagnosis and prognosis.

It remains clear that the predictability of changes to the amino acid sequence is practically nil as far as biological activities are concerned. The

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specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed amino acids in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which must be made in the amino acid sequence of SEQ ID NO: 2, which results in limited sequence identity and/or undefined substitutions and consequent use of these variants in the applications outlined in specification is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. Accordingly, the rejection is maintained and made.

5. The rejection of claims 84, 119, 121, 164, 210-214 and newly added claim 215 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

Applicants argue "[t]he term 'functional domain' is well known in the art, and refers to a region of a protein having a function...", see Remarks submitted July 12, 2005, page 38. Applicants allege they have provided Attachment B in support of their definition of domain. The Examiner has reviewed Applicants' arguments and points of view and finds them unpersuasive.

a. Claim 84 remains vague and indefinite in the recitation "a heterologous functional domain". While it is true one of ordinary skill in the art knows what a domain is this not the case when the language is "functional domain". What

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remains unclear is what functions should the domain possess. Accordingly, the metes and the bounds cannot be determined.

Claim Rejections - 35 USC § 102

6. The rejection of claims 84, 119, 121, 164, 165, 210-214 and newly added claim 215 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent application publication number US2002/0052308A1 (May 2, 2002) is maintained and made.

While Applicants acquiesce to the fact that the peptide epitope, I-121 to V-129, which is the same as Applicants' C35 peptide epitope, I-105 to V-113 of SEQ ID NO: 2 they state "[the] reference does not provide any description or suggestion of ITNSRPPCV peptide itself." These arguments have been carefully considered, but found unpersuasive.

The art clearly reads on Applicants' claims. Applicants' claims are very plainly and broadly set forth as a fusion protein comprising at least one C35 peptide epitope and a polypeptide selected from a group consisting of well known polypeptide sequences. Applicants should review the action mailed August 27, 2003 as Paper 22. Therein is the sequence alignment between Applicants' SEQ ID NO: 2 and the publication's SEQ ID NO: 966. The disclosed C35 peptide epitope is comprised amongst 122 additional amino acids, which reads on Applicants' claimed fusion protein. The rejection is maintained for the reasons established above and reasons of record.

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Allowable Subject Matter

7. Claims 123 (as it reads on species, nn. amino acids I-105 to V-113 of SEQ ID NO: 2), 158 and 166 are allowed.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm with alternate Fridays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER



Alana M. Harris, Ph.D.
27 September 2005